

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE
MEDICINE**

**NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY AND
ALTERNATIVE MEDICINE**

**MINUTES OF THE SIXTEENTH MEETING
January 30, 2004**

NACCAM Members Present

Dr. Zang-Hee Cho, Irvine, CA

Dr. Kristina Collins, McLean, VA

**Dr. Deborah J. Cotton, West Roxbury, MA

Dr. Jonathan Davidson, Durham, NC

Dr. Robert E. Fullilove, New York, NY

Dr. Murray Goldstein, Washington, DC

Dr. Michael Irwin, Los Angeles, CA

Dr. Alan I. Leshner, Washington, DC

Dr. Tieraona Low Dog, Albuquerque, NM

Dr. Barbara Timmerman, Tucson, AZ

Dr. Larry Walker, University, MS

*Dr. Diane Wara, San Francisco, CA

Dr. Benjamin Yang, San Francisco, CA

* Ad hoc members

** Participated by conference call

NACCAM Members Absent

Dr. Haile Debas, San Francisco, CA

Ex Officio Member Absent

COL Richard Niemtzwow, Clinton, MD

NIH Staff Present

National Center for Complementary and Alternative Medicine (NCCAM)

Ms. Willer Batten

Dr. Margaret Chesney, Deputy Director

Dr. Josh Berman

Ms. Alyssa Cotler

Dr. Dale Birkle

Mr. Jimmy Do

Dr. Marc Blackman

Ms. Karla Ehrler

Ms. Michelle Bolek

Ms. Linda Engel

Ms. April Bower

Ms. Carol Fitzpatrick

Mr. Brian Campbell

Ms. Anne Frost

Mr. Steve Casady

Dr. Martin Goldrosen

Dr. John Chah

Ms. Mary Gregg

Ms. Melinda Haskins
Ms. Carolyn Hodgkins
Ms. Camille Hoover
Ms. Jeanette Hosseini
Dr. Morgan Jackson
Ms. Rhoma Johnson
Mr. Roald Keith
Dr. Jack Killen
Dr. Jane Kinsel
Ms. Marguerite Klein
Ms. Robin Klevins
Ms. Karen Kun
Ms. Catherine Law
Mr. Qi-Ying Liu
Ms. Irimi Manoli
Dr. Kimberly McFann
Dr. Heather Miller
Ms. Ilze Mohseni

Ms. Barbara Moquin
Dr. Richard Nahin
Ms. Ellen O'Donnell
Ms. Donna Osborne
Dr. Nancy Pearson
Mr. Marc Pitts
Dr. Carol Pontzer
Ms. Linda Rich
Ms. Denise Simmonds-Barnes
Dr. Barbara Sorkin
Ms. Kathleen Stephan
Dr. Stephen Straus, Director
Ms. Jennifer Sutton
Ms. Chris Thomsen
Ms. Shirley Villone
Dr. Shan Wong
Ms. Angie Wongsam-Nollinger

Other NIH Employees

Ms. Iris Mikhail, National Cancer Institute
Mr. Dave Mineo, National Institute of Diabetes & Digestive & Kidney Diseases
Ms. Crystal Rosser, National Cancer Institute
Ms. Hasnaa Shafik, National Cancer Institute
Dr. Wendy Smith, National Cancer Institute
Ms. Mindy Staner, National Cancer Institute
Dr. Christine Swanson, Office of Dietary Supplements
Dr. Judith Vaitukaitis, National Center for Research Resources

Members of the Public

Ms. Shea Buckman
Ms. Kysa Christie
Dr. Steven Dentali
Mr. Michael Dyer
Mr. Andrew Hawkins
Ms. Laura Honesty
Ms. Amy Lange
Ms. Marilyn Mason
Mr. Michael May
Ms. Keekee Minor
Ms. Laura Morrill
Ms. Suzanne Niemeyer
Dr. Georgia Persinos
Ms. Chris Peterson

Ms. Elizabeth Sheley
Ms. Patricia Smith
Dr. Haidi Zhang

The National Advisory Council for Complementary and Alternative Medicine (NACCAM) began the closed session at 8:40 a.m. on January 30, 2004 at the National Institutes of Health (NIH) Neuroscience Conference Center in Rockville, Maryland. Dr. Jane Kinsel, Executive Secretary, called the meeting to order.

I. Closed Session

The first portion of the meeting was closed to the public in accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

A total of 234 applications were assigned to NCCAM. Of these, 177 were reviewed by The National Center for Complementary and Alternative Medicine (NCCAM), 56 by the Center for Scientific Review, and 1 by another institute. Applications that were noncompetitive, unscored, or were not recommended for further consideration by the scientific review groups were not considered by Council. Council agreed with staff recommendations on 4 applications and concurred on 157 applications requesting \$31,031,756 in total costs.

II. Open Session – Call to Order, Meeting Procedures

The open session of the NACCAM meeting convened at 12:45 p.m. Dr. Jane Kinsel, Executive Secretary, called the meeting to order. The members voted unanimously to approve the minutes of the previous meeting, which took place on September 8, 2003. Dr. Kinsel also made note of the dates of future Council meetings, and announced that a public comment session was scheduled for later in the afternoon.

III. Council Operating Procedures

Dr. Kinsel asked the Council to approve the Council Operating Procedures, which is done annually at each January Council meeting. Council voted unanimously to approve the procedures.

IV. Fifth Annual State of the Center Report

Dr. Stephen Straus, Director of NCCAM, presented the fifth annual State of the Center report, which included an overview of accomplishments and activities from 1999 to 2004.

Council and Staff Introductions

Dr. Straus introduced Dr. Robert Fullilove, a new Council member, who is from Columbia University, and Dr. Diane Wara, an ad hoc Council member, who is from the

University of California, San Francisco. He also announced that the Center had recently hired Dr. Qi-Ying Liu as a program officer and Dr. Jeanette Hosseini as a scientific review administrator. Mr. David Mineo, from NIDDK, is the acting grants management officer.

Budget Update

Dr. Straus updated the Council on the status of the budget. In FY 2004, NIH funding leveled off after experiencing a 5-year doubling period; during this time NCCAM's budget increased from \$50 million in FY 1999 to \$114.1 million in FY 2003. The final version of the FY 2004 appropriations bill allocates \$117.7 million for NCCAM. There will be some rescissions and a less than 1 percent contribution from each NIH institute and center to the NIH Roadmap initiative, resulting in an actual budget increase of about 2 percent.

Dr. Straus presented a graph that indicated roughly comparable NIH and NCCAM increases for the past 3 fiscal years. He noted that it is difficult to manage a portfolio with large budget fluxes. Another graph compared the grant success rates for NCCAM with NIH as a whole, measured as a percentage of funded projects compared to total number of scored applications. The NIH success rate is about 30 percent or slightly higher, whereas the NCCAM success rate has dropped from over 50 percent in 1999 to less than 15 percent in FY 2003.

General Research Overview

In 1999, the grants portfolio strategy involved building the NCCAM infrastructure by funding research centers, accepting relevant applications from other NIH institutes, and stimulating applications in selected areas through issuing Requests for Applications (RFAs). At that time, there were few applications being referred to NCCAM. A year later, NCCAM focused on stabilizing funding for the research centers program, setting priorities, creating an intramural program, and investing in training and careers.

In June 2002, an expert panel reviewed NCCAM's 12 P50 research centers and recommended a more flexible funding approach and a sharper focus on research. In September 2003, NCCAM awarded new center grants using the P01, U19, and R21 funding mechanisms. Similarly, in June 2003, an expert panel reviewed the six botanical centers funded by NCCAM, the Office of Dietary Supplements, and the National Institute of Environmental Health Sciences, and recommended more attention on preclinical research and early phase clinical studies under a P50 mechanism. Based on these recommendations, NCCAM and other NIH partners issued an RFA in December 2003 for funding the next round of botanical research centers.

As part of the NCCAM Research Centers Program, the Center recently approved its first awards under three major new initiatives: Centers of Excellence for Research on CAM (CERC), Developmental Centers for Research on CAM (DERC), and Planning Grants for International Research. The CERC awards were granted to Harvard University and Oregon State University, and the DERC awards went to Palmer Center for Chiropractic

Research and the New England School of Acupuncture. Finally, NCCAM made several awards to support planning grants for international centers.

Many clinical trials of CAM approaches reported in the literature do not involve the use of standardized and well characterized products. Therefore, to optimize research impact, NCCAM is putting greater emphasis on preclinical and early-phase clinical studies, working to design better clinical trials and obtaining well-characterized and standardized materials for clinical trials. In 2000, the NCCAM began funding research on botanical/drug interactions. To date, this research has yielded some critical findings. For example, St. John's wort was found to accelerate drug metabolism, thereby adversely affecting the efficacy of certain drugs. The PC-SPES issue of product contamination elevated product quality issues and how they are unique to CAM research. When PC-SPES was deemed contaminated, NCCAM terminated clinical trial work on the substance and revised plans to study it at the preclinical level.

A number of Phase III clinical studies are now being conducted on reliable products with co-funding from other NIH institutes and centers, and these trials reflect important public health priorities. NCCAM's Intramural Research Program (IRP) is supporting protocols designed to address current public health issues. For instance, the IRP has several studies on obesity, which include the study of insulin resistance, and ongoing or planned intervention studies using carnitine and ascorbic acid. Obesity research is a major focus of the Center's extramural program, too. In 2003, the results of a study co-funded by NCCAM, comparing a conventional diet with the Atkins diet, were published in the *New England Journal of Medicine*. Currently, NCCAM's priority areas include re-engineering the research centers programs; enhancing the NCCAM's training and career award programs and encouraging more research applications, particularly on botanicals; studying obesity; and studying brain-body interactions.

The following represent indices of NCCAM's success in its first 5 years: NCCAM built a center that is responsive to its mission, mindful of its resources, and fully integrated into NIH science and leadership. Further, the Center has created a successful CAM research and training collective; funded over 300 projects; published over 700 scientific publications; and informed public policy, patient choice, and clinical practice.

NCCAM's portfolio management tools help support the Center's current scientific priorities. The Center issued 4-year R01 awards, established differential paylines for R01s and R21s, negotiated some R01s downward, gained review and monitoring of all clinical trials by its Office of Clinical and Regulatory Affairs, closed underperforming programs, and aggressively leveraged funds.

NCCAM staff are active leaders and participants in the NIH Roadmap planning process. The benefits of doing so include access to an interdisciplinary collective for training and research as well as access to more sensitive technologies, research tools, services, and patient communities.

NCCAM has one of the two lowest paylines of any institute or center within NIH. As a result, potential applicants are becoming discouraged and submitting their proposals to other institutes and centers. Moreover, it remains a challenge to facilitate the movement of successful R21 recipients to their first R01 award. Further, the proportion of active R01 and R21 awards has changed, from more R01s in the Center's early years to more R21s in the last 2 years. With a 2 percent projected budget increase, the number of NCCAM grant awards is projected to decrease slightly.

In the first 5-year plan, NCCAM identified its strategic areas as investing in research, training CAM investigators, expanding outreach, and facilitating integration. The next 5-year plan will highlight the Center's interest in maintaining current strategic areas, reviewing and critiquing progress to date, making changes based on lessons learned, providing greater specificity, and prioritizing investments according to opportunities for greatest success and impact. In January 2005, Dr. Straus plans to announce the next 5-year strategic plan.

Council Discussion

Dr. Leshner noted that many people use CAM approaches because of disability, rather than to prevent illness or death. Dr. Straus said that NCCAM supports research on chronic and debilitating conditions, such as pain and mental health, as well as on those which can lead to death, such as heart disease and cancer.

Dr. Goldstein strongly encouraged NCCAM to effectively engage organized professional and clinical care groups and other stakeholders in developing the strategic plan. These groups could also help to more widely disseminate information about the plan. Dr. Straus noted that input will be solicited through a number of ways, including regional public forums and a strategic planning workshop scheduled for May 2004, and that NCCAM will continue to explore ways to successfully involve stakeholders.

In response to a question about intellectual property, Dr. Straus noted that many CAM treatments are in the public domain and, therefore, not patentable. As a result, there is a lack of incentive for companies to do research. For example, dose-ranging studies of a botanical product are critical before proceeding to a large clinical trial. Studies of a good but diluted product can fail if an optimal dose is not used. Dr. Straus said that NCCAM invests in pursuing and developing high-quality products and determining an appropriate dose. Dr. Cho suggested that CAM research could benefit from the use of increasingly complicated and expensive new technologies.

V. Overview of the National Center for Research Resources (NCRR)

Dr. Straus introduced Dr. Judith Vaitukaitis, director of NCRR, who provided an overview of the Center's activities. NCRR has four extramural divisions: biomedical technology, clinical research resources, comparative medicine, and research infrastructure. NCRR just completed its third 5-year strategic plan, and has a budget this year of just under \$1.2 billion. All of the Center's undertakings must be science-driven

initiatives. Previously, clinical research constituted 80 percent of the annual budget; it now represents 31 percent because other areas have grown.

Dr. Vaitukaitis offered examples of opportunities for close collaboration between NCRR and NCCAM, including one research project—a multi-faceted study set in states with high Native American and Eskimo populations—that has an indigenous medicine aspect.

Dr. Vaitukaitis provided examples of how NCRR makes equipment available to researchers. Through its Shared Instrumentation Grant Program, typically involving 15 or more researchers, the Center provides funding up to \$500,000 for “off-the-shelf” instrumentation that is too expensive to purchase with research project grant funding. The shared instruments in the program include confocal microscopes, NMR imagers, mass spectrometers, protein/DNA sequencers, and other technology. Complementing this, the High End Instrumentation Program accepts applications from medical schools and hospitals for larger equipment such as bioimagers, mass spectrometers, supercomputers, NMR spectrometers, and other technologies. The National Center for Microscopy and Imaging Research, which operates over the Internet under the Division of Biomedical Technology, offers workshops to help investigators learn about the equipment and its limitations and provides researchers access to microscopes, synchrotrons, and other technologies. Researchers ship their samples to a specific location, and receive information about viewing their work online; additional testing can be done if needed. The program enhances access to technology and research expertise, and is cost-effective.

Future areas of emphasis for NCRR include multi-disciplinary teams, integrative or systems approaches more dependent on technologies, and information management. Research is becoming more multidisciplinary, with an integrative or systems approach. NCRR hopes to continue providing access to advanced instrumentation and technologies, with greater use of the Internet, bioinformatics, and other tools essential for future research. Much of the emphasis will be on collaboration. Research networks help to facilitate studies of obesity, diabetes, virtual cells, neuroscience test bed, and autoimmune disorders. NCRR hopes to make more expertise available over the Internet. They will continue to focus on configuring ongoing and new research optimally, defining categorical research centers in the networks, transcending the entire spectrum of clinical research, and melding networks together.

VI. Role of GCRCs – Launching New Areas of Research

Dr. Diane Wara, Professor of Pediatrics at the University of California, San Francisco, provided an overview of the General Clinical Research Centers (GCRCs). Through NCRR, NIH has funded 80 GCRCs. The national program has new areas of emphasis, including multi-disciplinary work, use of high technology, and integration of basic and clinical science. Historically, however, the great benefit of the GCRCs is that they provide an envelope of resources to an institution that are greater than those available to individual investigators. There has been a decrease in the number of trained clinical

investigators in the United States. People do clinical research for a number of reasons: to translate basic research discoveries to the bedside; to develop cost-effective health care; to develop disease-prevention strategies; to introduce these strategies to the public; and to change public policy. These last two areas deserve special emphasis.

GCRCs were initiated in the 1960s to provide extramural investigators the infrastructure for conducting clinical investigations. Through 1985, the focus was on physiology/endocrinology studies of in-patients. Since then, other areas of investigation have been added, such as AIDS, cancer, and genetics, as well as increased patient treatment in an outpatient setting. The trend is likely to continue, resulting in more patients in the community. The GCRCs 1) provide institutional resources for both inpatient and outpatient research, 2) host investigations by a variety of research entities, 3) provide specialized medical personnel such as research nurses and dieticians, and 4) offer specialized laboratories and computerized database management.

There are three GCRCs in San Francisco. The pediatrics program at UCSF, which is in its 22nd year of funding, pays for space, nurses' salaries, and a variety of other costs. There are 77 active protocols and 178 investigators with over \$40 million in peer-reviewed funding. The center encompasses the Schools of Medicine, Dentistry, and Nursing. Anyone at UCSF can use the center for research on children and youths. Promising research areas include the molecular basis of disease, pharmacogenomics and pharmacogenetics, neuroscience, stem-cell biology, and epidemiological research with molecular and genetic tools.

At the other extreme of life, there are studies of conditions of the "healthy aged": arthritis, osteoporosis, poor nutrition, and decreased vision. GCRCs can research this population in the community, use multi-disciplinary collaboration, employ extended technology, and intervene with exercise physiology and nutritional change. Common disorders that lend themselves to study by GCRCs include asthma and obesity. It is important to study patients living in the community. The Institute of Medicine sees GCRCs as the logical means for bringing together laboratory research and human studies.

VII. Concept Clearance – GCRC CAM Research Program

Dr. Richard Nahin presented a concept for supplements to the GCRCs for CAM research. Data show that GCRCs have supported a variety of CAM projects, although the number of projects fluctuates from year to year. Broken out by modality, most projects are biologically-based, with the second highest number in the mind-body area.

The goal of this initiative is to stimulate GCRCs to conduct research on CAM. With the considerable resources, infrastructure, staffing, and patient populations provided by the GCRCs, the primary funding from this initiative would be for investigator time. The initiative is expected to facilitate and expand the evaluation of CAM treatments for a wide range of diseases and conditions currently being evaluated at GCRCs. Preliminary

data generated by the initiative will be the basis for further, more ambitious research studies, including clinical trials.

The initiative will solicit projects from GCRCs to conduct clinical investigation of CAM treatments. Qualified CAM practitioners must be active members of an interdisciplinary team, and each applicant must consider how a CAM research program will affect their communities, especially minority and under-served populations. The initiative would provide funds to stimulate interest and leverage funds with NCCR. The R03 and R21 mechanisms are proposed for 3-year awards.

There was discussion among the Council members regarding whether to develop a training endeavor within the GCRC that would train investigators in research on CAM. Dr. Chesney suggested instead that DERT staff would make explicit suggestions to encourage applicants to use the GCRCs in conjunction with the K award program, designed for students to work with mentors who already have a study.

Council voted approval of the concept, provided that the initiative was issued as a program announcement rather than an RFA.

VIII. Concept Clearance – Improving Measures of Hot Flashes

Dr. Heather Miller presented a concept addressing the measurement of hot flashes in women. Many women are using CAM to manage hot flashes, but the clinical studies to date on CAM use for hot flashes have been small and short-term, producing equivocal findings. Since many CAM therapies produce small effects relative to estrogen and since women underreport hot flashes in ambulatory studies, researchers are faced with the need for very large numbers of subjects or improved measures of hot flashes. In collaboration with eight other NIH institutes, centers, and offices, NCCAM convened a 1-day workshop on January 20, 2004 to assess existing measures of hot flashes and to discuss approaches to improving them.

Dr. Miller summarized highlights from the workshop. There are two basic strategies for measuring hot flashes: subjective self-reported data and objective measures, such as sternal skin conductance monitoring. Compared to objective measures, women participating in ambulatory studies can miss as many as 65 percent of hot flashes detected by sternal skin conductance.

The workshop attendees concluded that improving measures of hot flashes requires improved knowledge in several areas, including 1) the physical processes underlying hot flashes, 2) improved sternal skin conductance systems, 3) performance characteristics of questionnaires and diaries to collect self-reported data on hot flash frequency, 4) improved and validated instruments for collecting data on intensity and interference with daily activities, 5) the mechanisms of action of placebos, and 6) animal models. Dr. Miller is writing a meeting summary that will be disseminated on the NIH website.

The objectives of the proposed initiative may include the following:

- To identify additional physiologic markers of hot flashes and develop tools to measure them that are suitable in ambulatory studies
- To improve sensitivity and specificity of self-reported subjective measures
- To improve basic understanding of hot flashes and the placebo effect reported in most clinical studies
- To develop animal models of hot flashes to screen the myriad of CAM modalities proposed to manage hot flashes and the basic mechanisms associated with hot flashes

Dr. Straus said that NCCAM was invited to join an NIH meeting held in November 2002 on the results of the Women's Health Initiative (WHI) because women were turning to CAM for relief of symptoms. Small studies have been done; the next step is to conduct large studies or to study smaller numbers of participants using more sensitive measurements. In response to a question about whether the initiative was only about measurement, or if it also included research, Dr. Miller said that it covered both.

Dr. Miller commented that a number of CAM therapies, such as black cohosh, are being marketed and used to treat hot flashes. Also being used are traditional Chinese medicine, acupuncture, and biofeedback. These systems are less effective than estrogen at reducing hot flashes. However, for some women, some decrement may be enough. The first need is for greater sensitivity in measurement to assess the efficacy of these therapies. Additional work is also needed to assess safety.

It was suggested that the WHI or the Office of Research on Women's Health should take the lead on developing improved measures, since this issue transcends NCCAM. Dr. Straus noted that NCCAM wants to take a proactive approach given the prevalence of use of CAM therapies for management of the menopausal transition. However, NCCAM will work with other NIH institutes and centers in the development of the initiative.

This initiative relates to the NIH Roadmap theme of improving measurements of biobehavioral phenomena. It is likely that by mid-2005 there will be a strong recommendation to do more for women with post-menopausal symptoms, and NCCAM wants to be poised to respond.

Council unanimously approved the concept.

IX. Public Comment Session

No members of the public came forward to speak during this session.

X. Adjournment

Dr. Straus adjourned the meeting at 4:10 p.m.